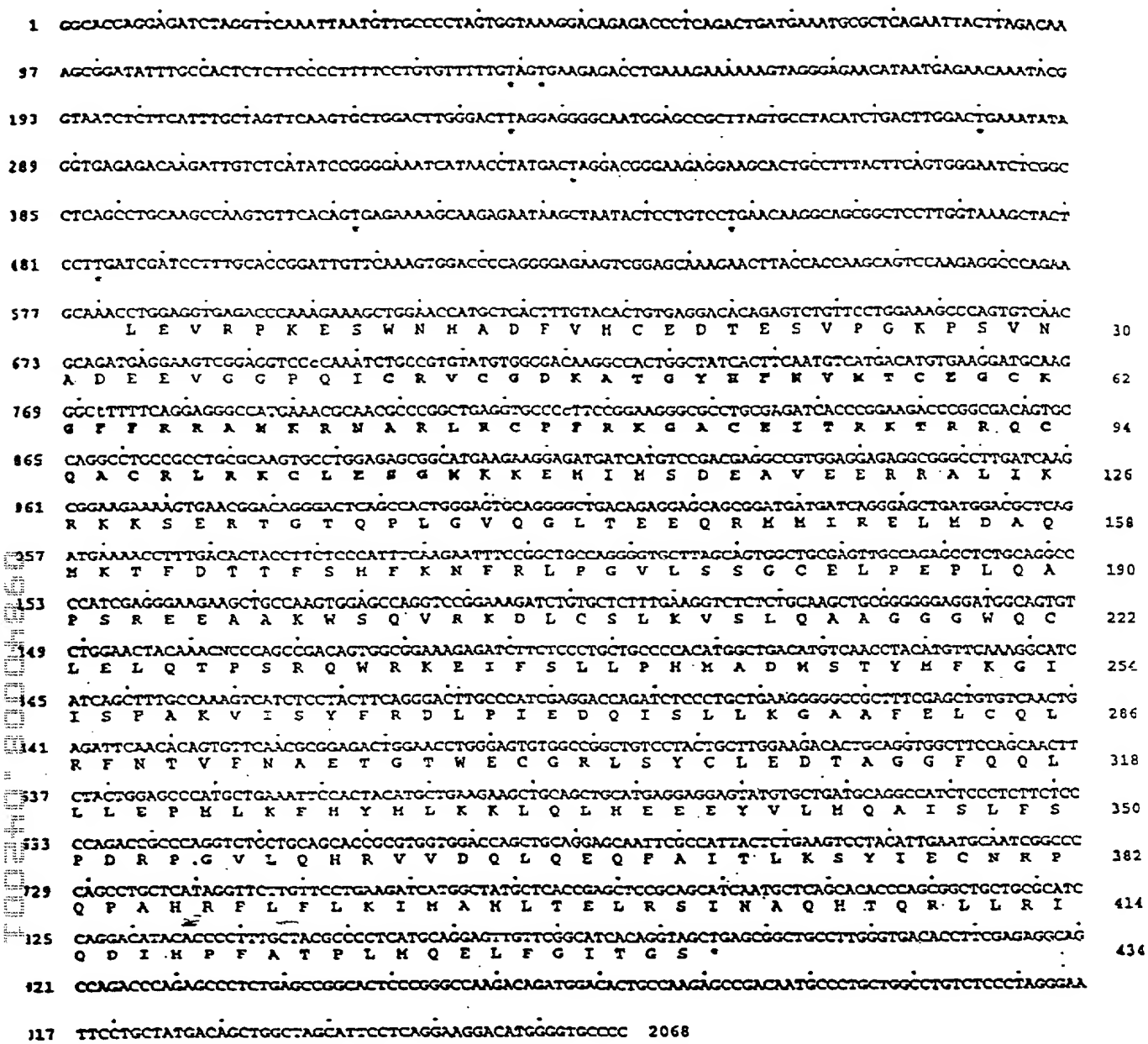
1 GGCACCAGGAGATCTAGGTTCAAATTAATGTTGCCCCTAGTGGTAAAGGACAGAGACCCTCAGACTGATGAAATGCGCTCAGAATTACTTAGACAA
97 AGCGGATATTTGCCACTCTCTTCCCCTTTTCCTGTGTTTTTGTAGTGAAGAGACCTGAAAGAAAAAAGTAGGGAGAACATAATGAGAACAAATACG
193 GTAATCTCTTCATTTGCTAGTTCAAGTGCTGGACTTGGGACTTAGGAGGGGCAATGGAGCCGCTTAGTGCCTACATCTGACTTGGACTGAAATATA
289 GGTGAGAGACAAGATTGTCTCATATCCGGGGAAATCATAACCTATGACTAGGACGGGAAGAGGAAGCACTGCCTTTACTTCAGTGGGAATCTCGGC
385 CTCAGCCTGCAAGCCAAGTGTTCACAGTGAGAAAAGCAAGAGAATAAGCTAATACTCCTGTCCTGAACAAGGCAGCGGCTCCTTGGTAAAGCTACT
481 CCTTGATCGATCCTTTGCACCGGATTGTTCAAAGTGGACCCCAGGGGAGAAGTCGGAGCAAAGAACTTACCACCAAGCAGTCCAAGAGGCCCAGAA
577 GCAAACCTGGAGGTGAGACCCAAAGAAAGCTGGAACCATGCTCACTTTGTACACTGTGAGGACACAGAGTCTGTTCCTGGAAAGCCCAGTGTCAAC
L E V R P K E S W N H A D F V H C E D T E S V P G K P S V N 30
673 GCAGATGAGGAAGTCGGAGGTCCCCAAATCTGCCGTGTATGTGGCGACAAGGCCACTGGCTATCACTTCAATGTCATGACATGTGAAGGATGCAAG
A D E E V G G P Q I C R V C G D K A T G Y H F N V M T C E G C K 62
769 GGCTTTTTCAGGAGGGCCATGAAACGCAACGCCCGGCTGAGGTGCCCCTTCCGGAAGGGCGCCTGCGAGATCACCCGGAAGACCCGGCGACAGTGC
G F F R R A M K R N A R L R C P F R K G A C E I T R K T R R Q C 94
865 CAGGCCTCCCGCCTGCGCAAGTGCCTGGAGAGCGGCATGAAGAAGGAGATGATCATGTCCGACGAGGCCGTGGAGGAGAGGCGGGCCTTGATCAAG
Q A C R L R K C L E S G M K K E M I M S D E A V E E R R A L I K 126
961 CGGAAGAAAAGTGAACGGACAGGGACTCAGCCACTGGGAGTGCAGGGGCTGACAGAGGAGCAGCGGATGATGATCAGGGAGCTGATGGACGCTCAG
R K K S E R T G T Q P L G V Q G L T E E Q R M M I R E L M D A Q 158
1057 ATGAAAACCTTTGACACTACCTTCTCCCATTTCAAGAATTTCCGGCTGCCAGGGGTGCTTAGCAGTGGCTGCGAGTTGCCAGACCCTCTGCAGGCC
M K T F D T T F S H F K N F R L P G V L S S G C E L P E P L Q A 190
1153 CCATCGAGGGAAGAAGCTGCCAAGTGGAGCCAGGTCCGGAAAGATCTGTGCTCTTTGAAGGTCTCTCTGCAAGCTGCGGGGGGAGGATGGCAGTGT
P S R E E A A K W S Q V R K D L C S L K V S L Q A A G G G W Q C 222
1249 CTGGAACTACAAACNCCCAGCCGACAGTGGCGGAAAGAGATCTTCTCCCTGCTGCCCCACATGGCTGACATGTCAACCTACATGTTCAAAGGCATC
L E L Q T P S R Q W R K E I F S L L P H M A D M S T Y M F K G I 254
1345 ATCAGCTTTGCCAAAGTCATCTCCTACTTCAGGGACTTGCCCATCGAGGACCAGATCTCCCTGCTGAAGGGGGCCGCTTTCGAGCTGTGTCAACTG
I S P A K V I S Y F R D L P I E D Q I S L L K G A A F E L C Q L 286
1441 AGATTCAACACAGTGTTCAACGCGGAGACTGGAACCTGGGAGTGTGGCCGGCTGTCCTACTGCTTGGAAGACACTGCAGGTGGCTTCCAGCAACTT
R F N T V F N A E T G T W E C G R L S Y C L E D T A G G F Q Q L 318
1537 CTACTGGAGCCCATGCTGAAATTCCACTACATGCTGAAGAAGCTGCAGCTGCATGAGGAGGAGTATGTGCTGATGCAGGCCATCTCCCTCTTCTCC
L L E P M L K F H Y M L K K L Q L H E E E Y V L M Q A I S L F S 350
1633 CCAGACCGCCCAGGTCTCCTGCAGCACCGCGTGGTGGACCAGCTGCAGGAGCAATTCGCCATTACTCTGAAGTCCTACATTGAATGCAATCGGCCC
P D R P G V L Q H R V V D Q L Q E Q F A I T L K S Y I E C N R P 382
1729 CAGCCTGCTCATAGGTTCTTGTTCCTGAAGATCATGGCTATGCTCACCGAGCTCCGCAGCATCAATGCTCAGCACACCCAGCGGCTGCTGCGCATC
Q P A H R F L F L K I M A M L T E L R S I N A Q H T Q R L L R I 414
1825 CAGGACATACACCCCTTTGCTACGCCCCTCATGCAGGAGTTGTTCGGCATCACAGGTAGCTGAGCGGCTGCCTTGGGTGACACCTTCGAGAGGCAG
Q D I H P F A T P L M Q E L F G I T G S * 434
1921 CCAGACCCAGAGCCCTCTGAGCCGGCACTCCCGGGCCAAGACAGATGGACACTGCCAAGACCCGACAATGCCCTGCTGGCCTGTCTCCCTAGGGAA
2017 TTCCTGCTATGACAGCTGGCTAGCATTCCTCAGGAAGGACATGGGGTGCCCC 2068

FIG. 1A

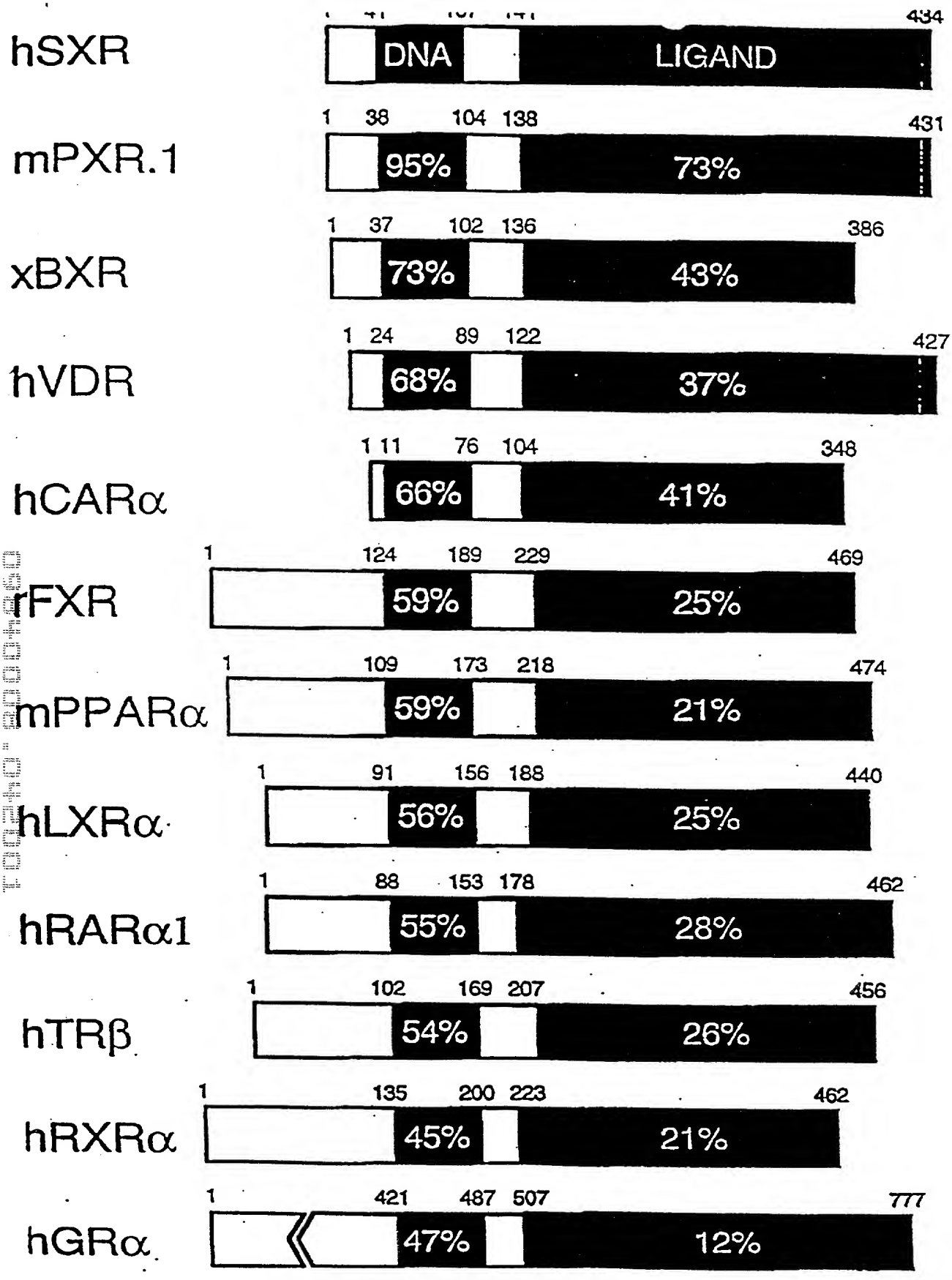
hSXR
434
DNA
LIGAND
mPXR.1
1 38 104 138
431
95%
73%
xBXR
1 37 102 136
386
73%
43%
hVDR
1 24 89 122
427
68%
37%
hCARα
1 11 76 104
348
66%
41%
rFXR
1 124 189 229
469
59%
25%
mPPARα
1 109 173 218
474
59%
21%
hLXRα
1 91 156 188
440
56%
25%
hRARα1
1 88 153 178
462
55%
28%
hTRβ
1 102 169 207
456
54%
26%
hRXRα
1 135 200 223
462
45%
21%
hGRα
1 421 487 507
777
47%
12%

FIG. 1B

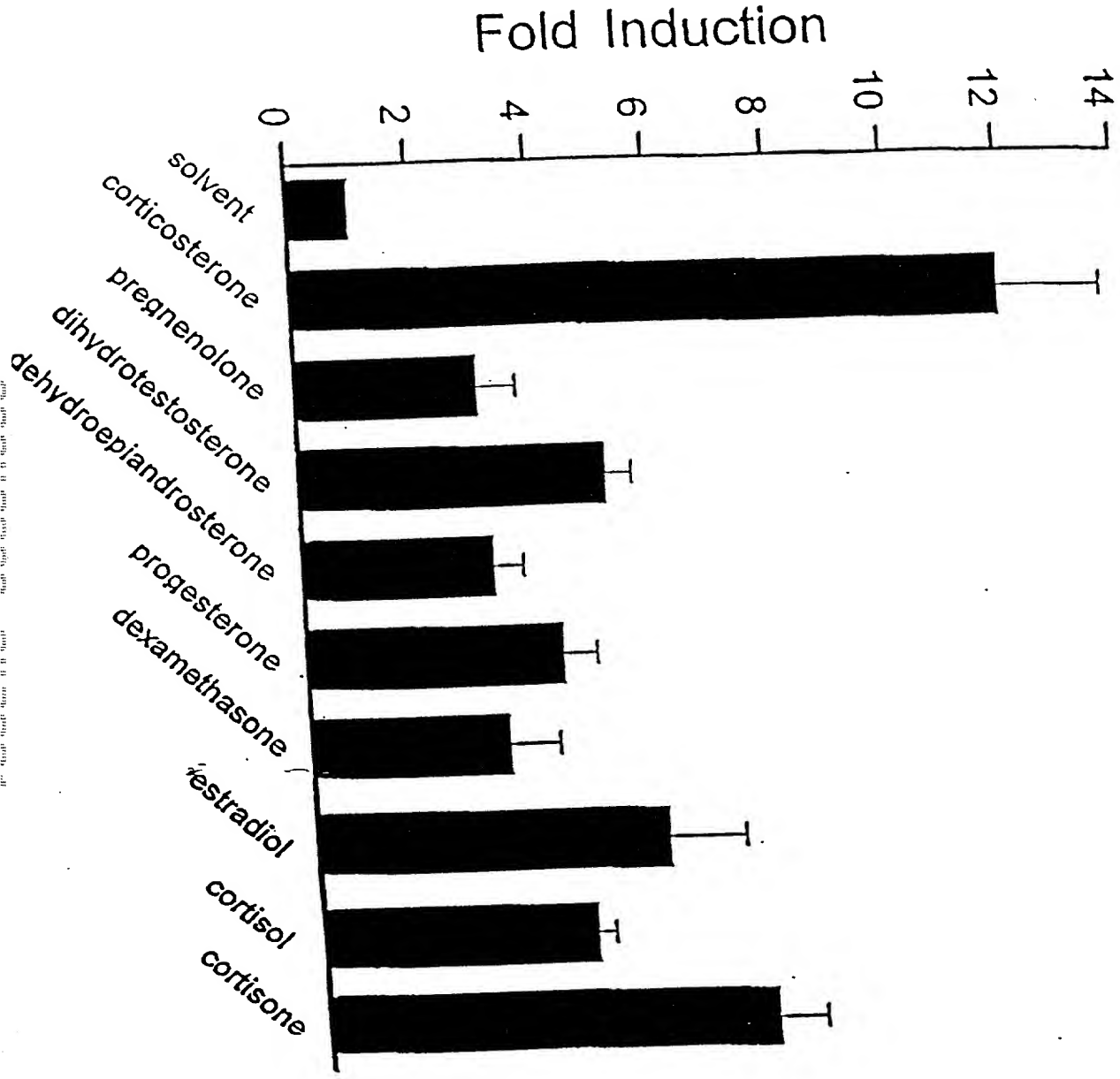
Fold Induction
0
2
4
6
8
10
12
14
solvent
corticosterone
pregnenolone
dihydrotestosterone
dehydroepiandrosterone
progesterone
dexamethasone
*estradiol
cortisol
cortisone

FIG. 2

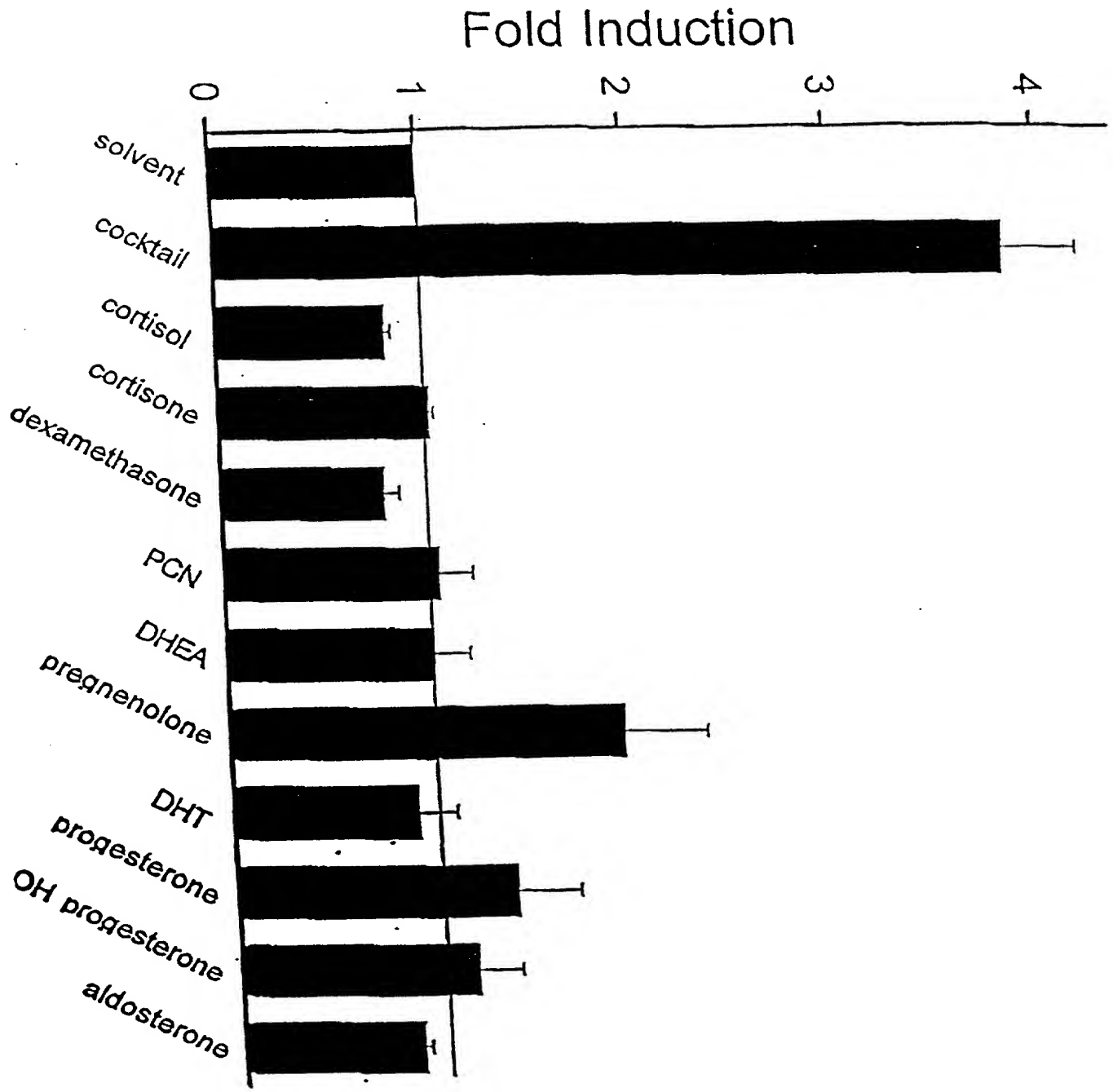
Fold Induction
0
1
2
3
4
solvent
cocktail
cortisol
cortisone
dexamethasone
PCN
DHEA
pregnenolone
DHT
progesterone
OH progesterone
aldosterone

FIG. 3

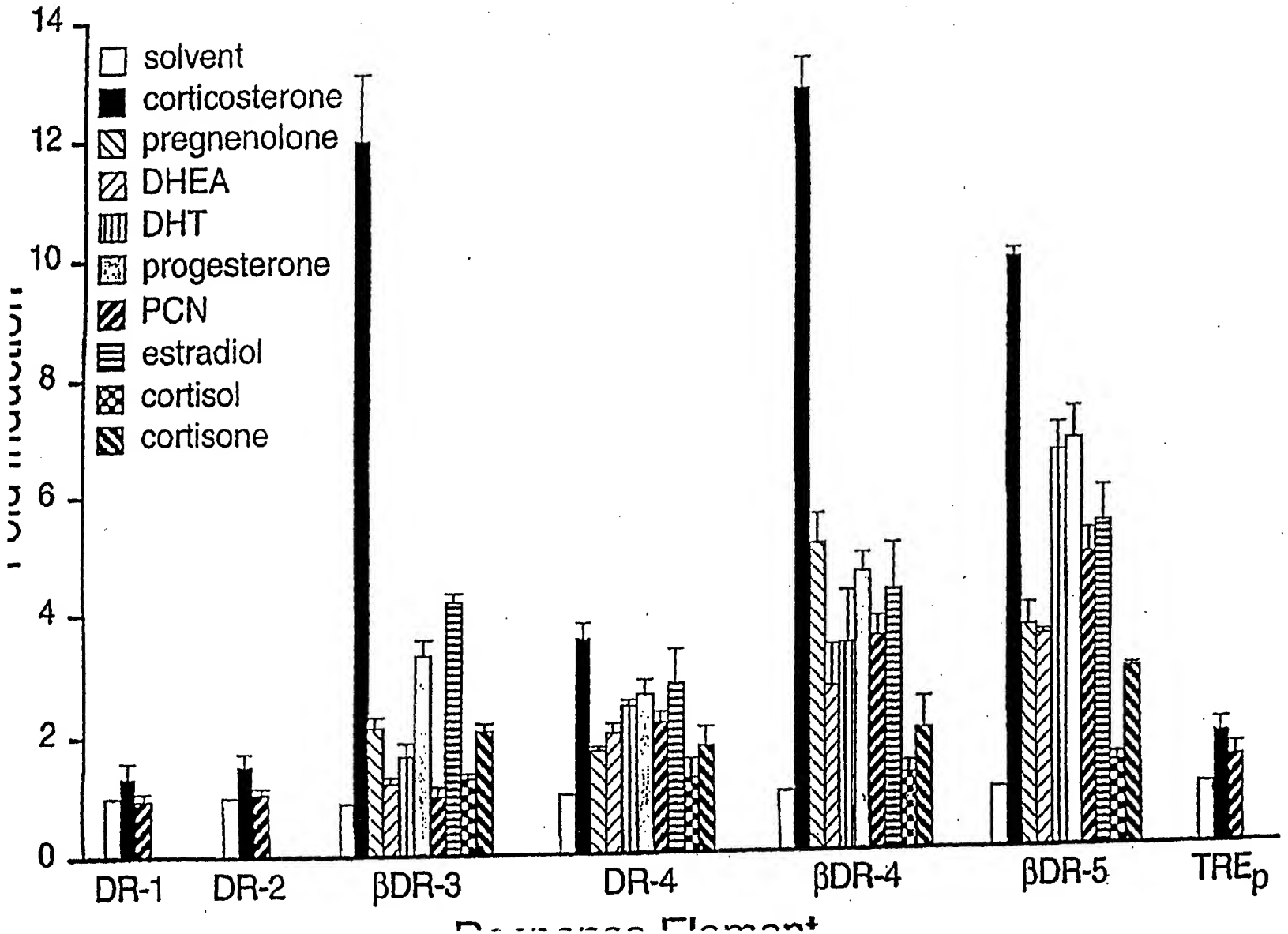
14
12
10
8
6
4
2
0
solvent
corticosterone
pregnenolone
DHEA
DHT
progesterone
PCN
estradiol
cortisol
cortisone
DR-1
DR-2
βDR-3
DR-4
βDR-4
βDR-5
TREp

FIG. 4

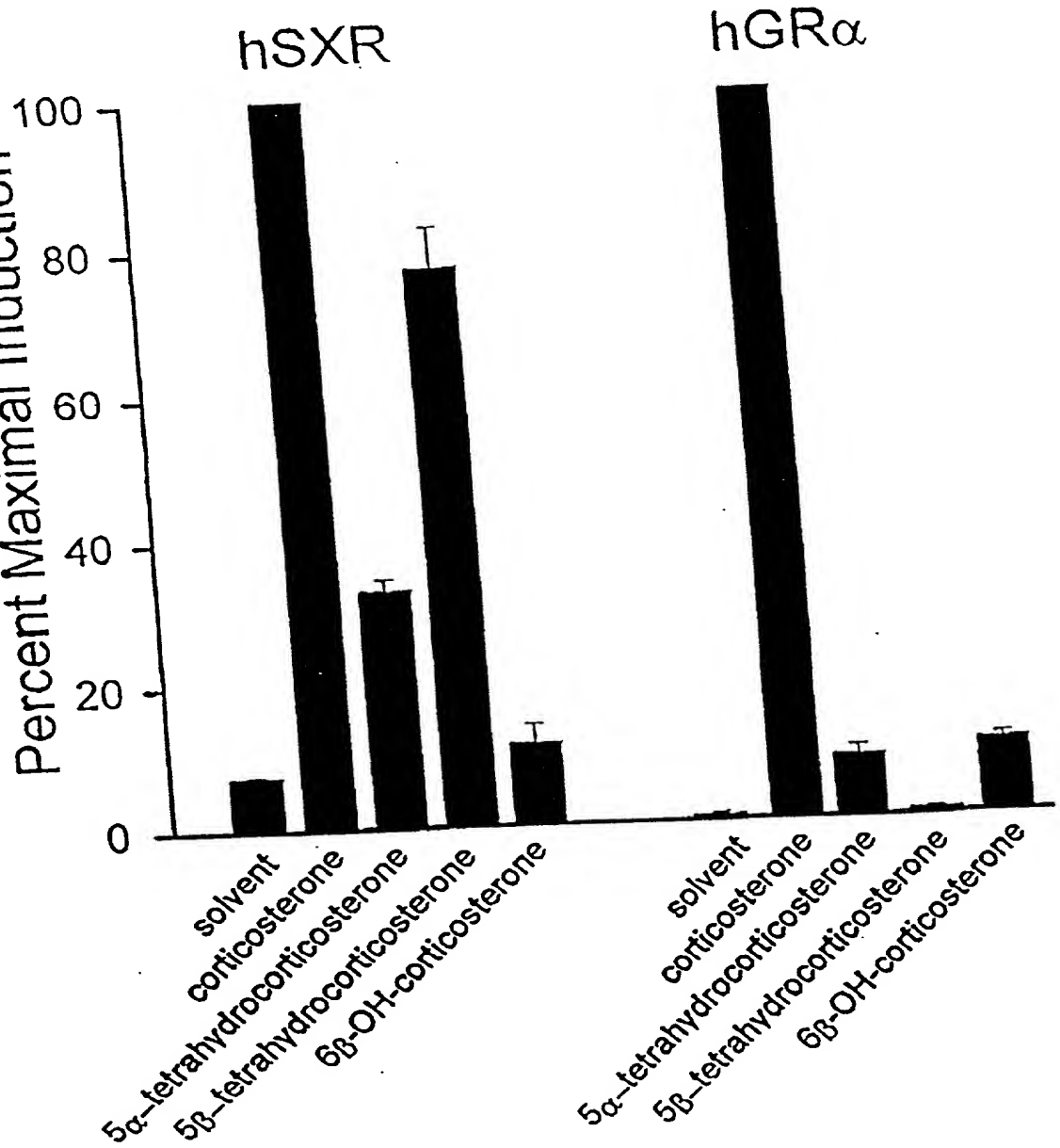
hSXR
hGRα
Percent Maximal Induction
100
80
60
40
20
0
solvent
corticosterone
5α–tetrahydrocorticosterone
5β–tetrahydrocorticosterone
6β-OH-corticosterone
solvent
corticosterone
5α–tetrahydrocorticosterone
5β–tetrahydrocorticosterone
6β-OH-corticosterone

FIG. 5

DR-3	
rCYP3A1	tagac **AGTTCA** tga **AGTTCA** tctac
rCYP3A2	taagc **AGTTCA** taa **AGTTCA** tctac
rUGT1A6	actgt **AGTTCA** taa **AGTTCA** catgg
DR-4	
rbCYP2C1	caatc **AGTTCA** acag **GGTTCA** ccaat
rP450R	cac **AGGTGA** gctg **AGGCCA** gcagc **AGGTCG** aaa
DR-5	
rCYP2A1	gtgca **GGTTCA** actgg **AGGTCA** acatg
rCYP2A2	gtgct **GGTTCA** actgg **AGGTCA** gtatg
rCYP2C6	agtct **AGTTCA** gtggg **GGTTCA** gtctt
hCYP2E1	gagat **GGTTCA** aggaa **GGGTCA** ttaac

FIG. 6A

CYP3A4	tagaata **TGAACT** caaagg **AGGTCA** gtgagtgg
CYP3A5	tagaata **TGAACT** caaagg **AGGTAA** gcaaaggg
CYP3A7	tagaata **TTAACT** caatgg **AGGC.A** gtgagtgg

FIG. 6B

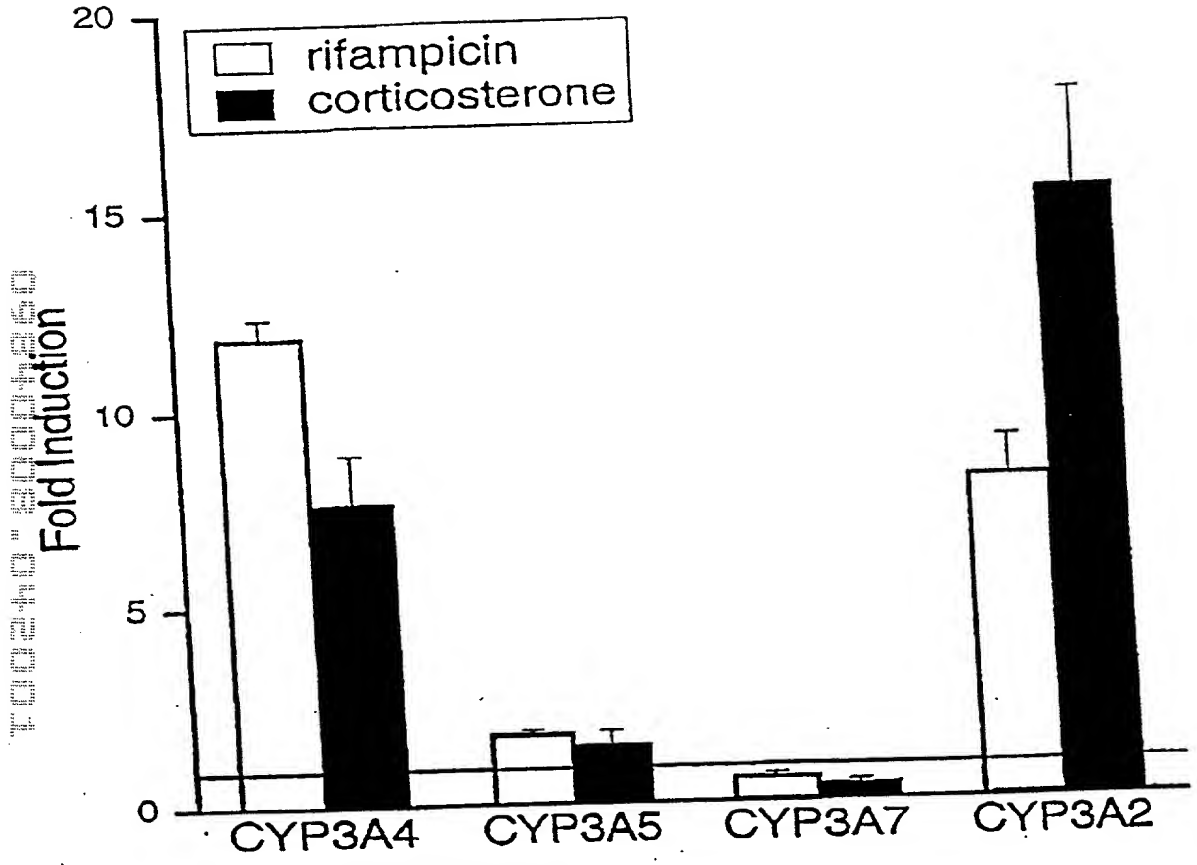
rifampicin
corticosterone
Fold Induction
20
15
10
5
0
CYP3A4
CYP3A5
CYP3A7
CYP3A2

FIG. 6C

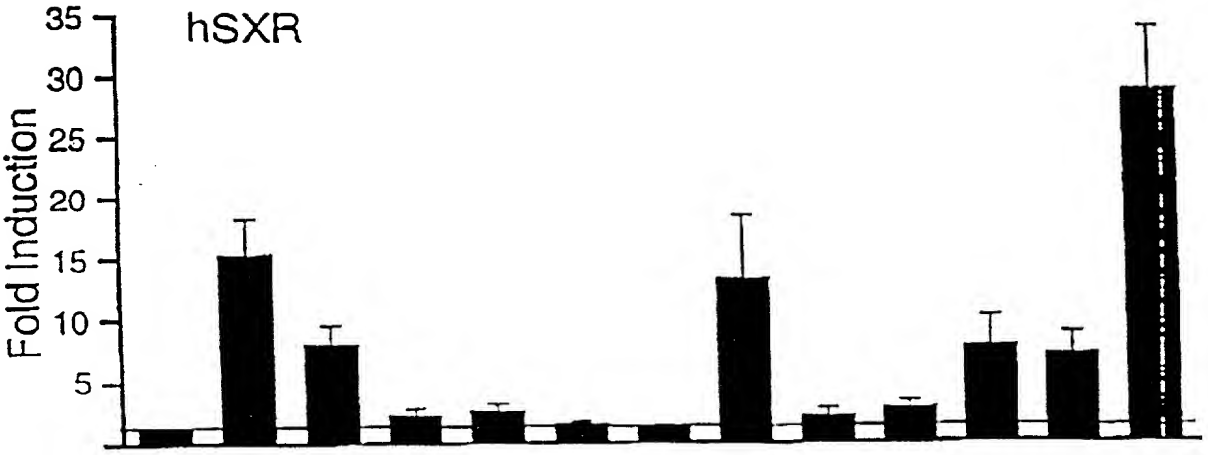

FIG. 7A

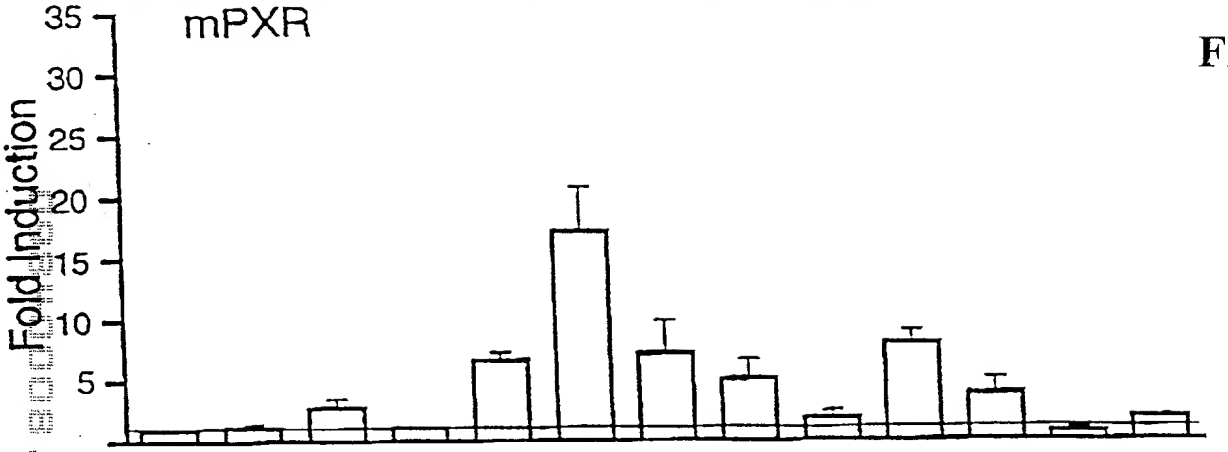

FIG. 7B

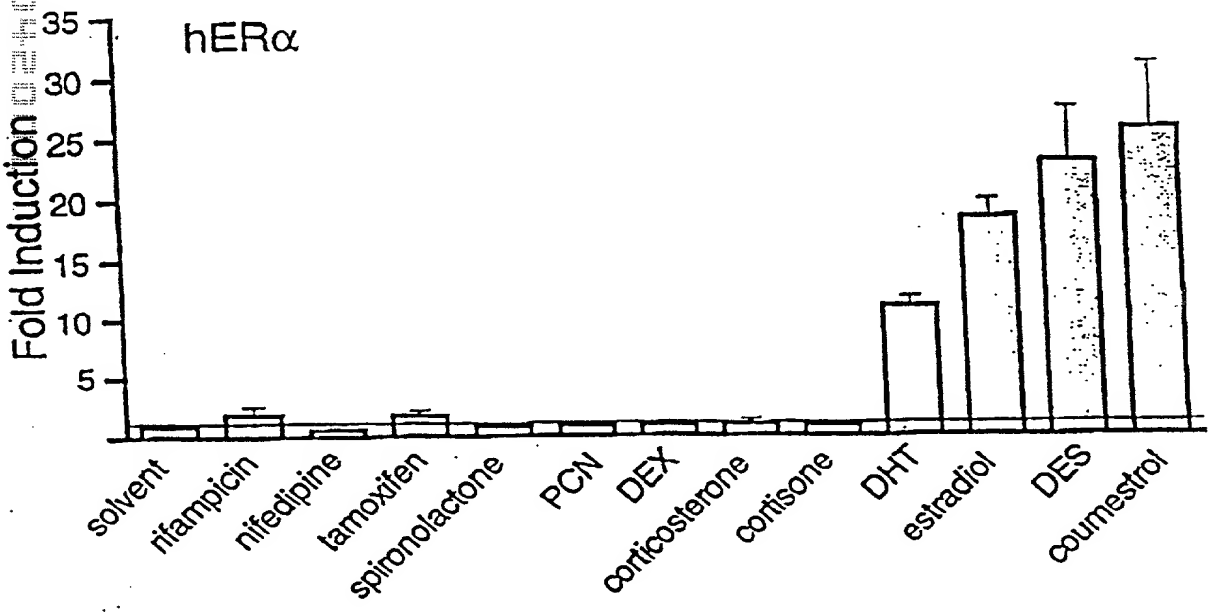

FIG. 7C

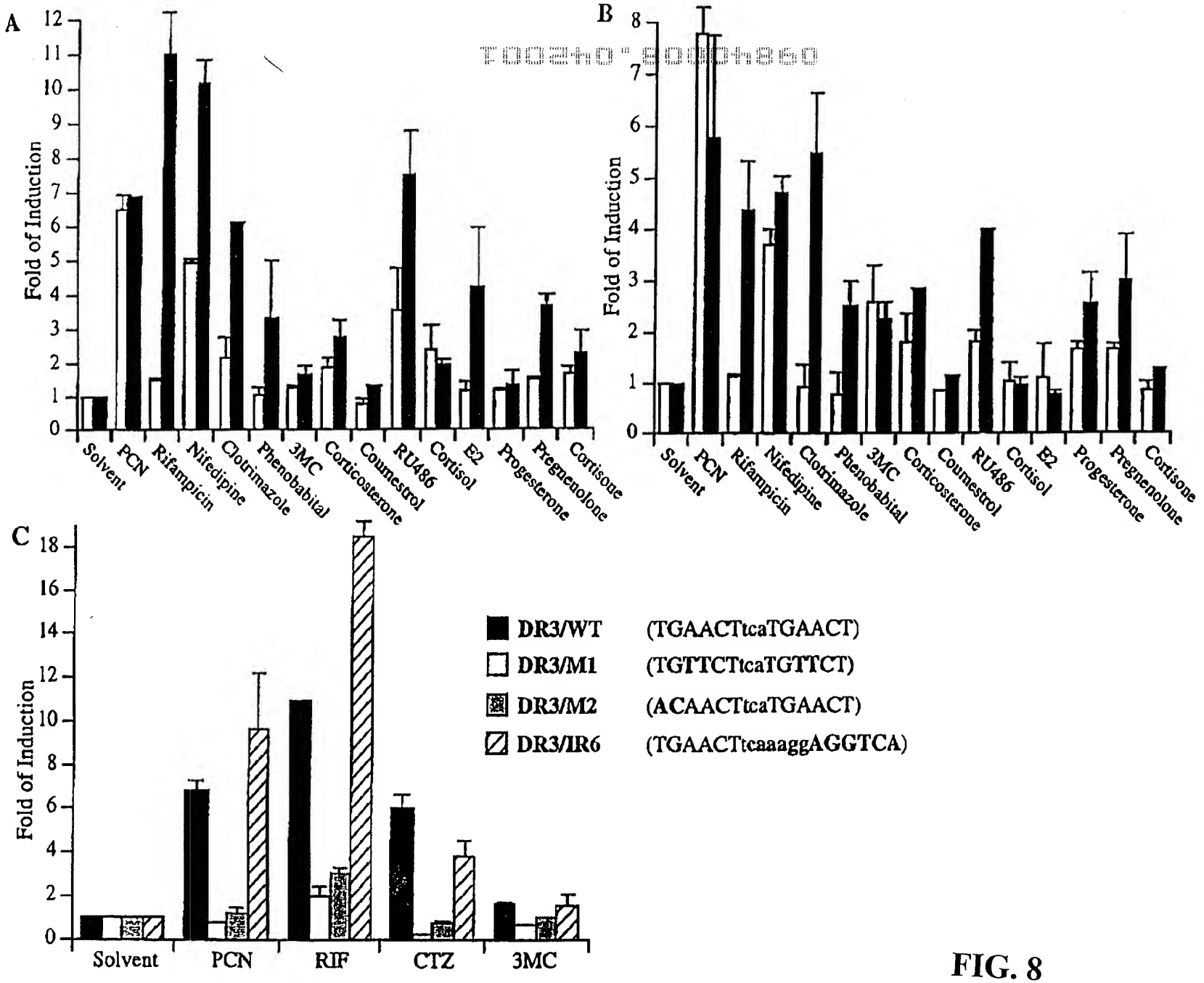
A
Fold of Induction
Solvent
PCN
Rifampicin
Nifedipine
Clotrimazole
Phenobabital
3MC
Corticosterone
Coumestrol
RU486
Cortisol
E2
Progesterone
Pregnenolone
Cortisone
B
Fold of Induction
Solvent
PCN
Rifampicin
Nifedipine
Clotrimazole
Phenobabital
3MC
Corticosterone
Coumestrol
RU486
Cortisol
E2
Progesterone
Pregnenolone
Cortisone
C
Fold of Induction
Solvent
PCN
RIF
CTZ
3MC
DR3/WT (TGAACTtcaTGAACT)
DR3/M1 (TGTTCTtcaTGTTCT)
DR3/M2 (ACAACTtcaTGAACT)
DR3/IR6 (TGAACTtcaaaggAGGTCA)

FIG. 8

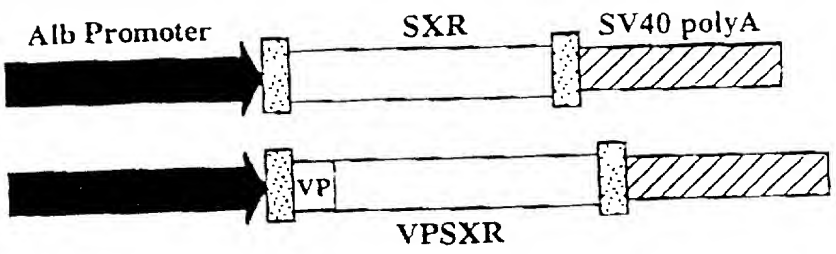
Alb Promoter
SXR
SV40 polyA
VP
VPSXR

FIG. 9

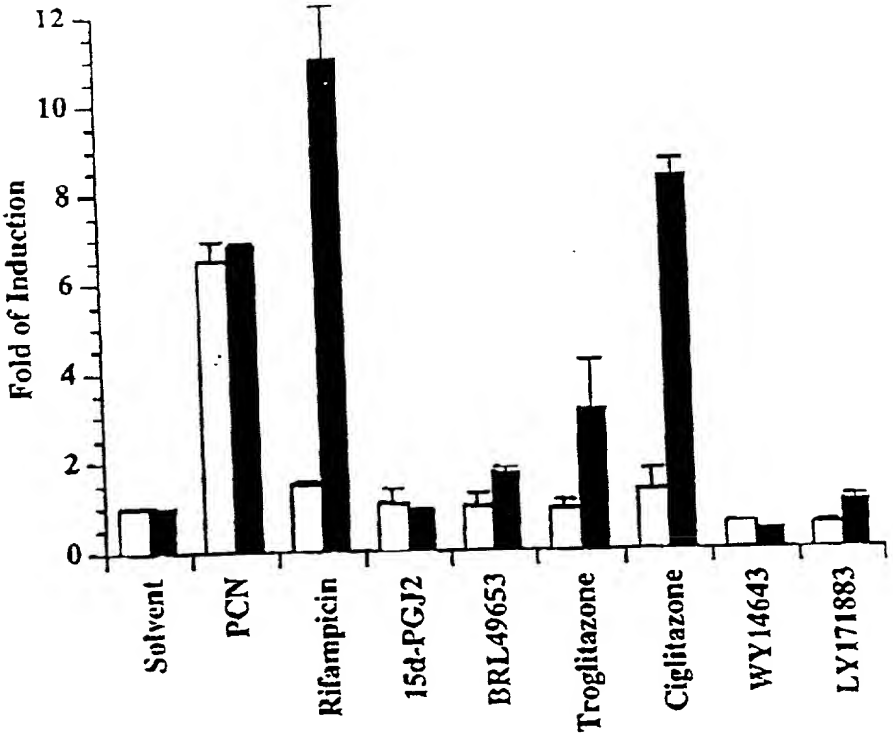
Fold of Induction
0
2
4
6
8
10
12
Solvent
PCN
Rifampicin
15d-PGJ2
BRL49653
Troglitazone
Ciglitazone
WY14643
LY171883

FIG. 10

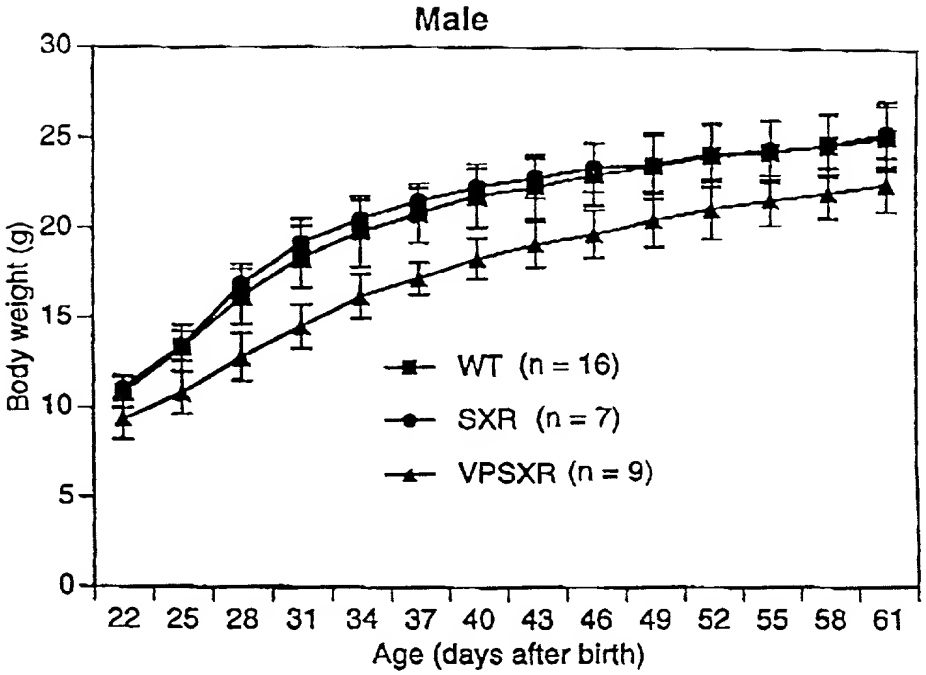
Male
Body weight (g)
30
25
20
15
10
5
0
22 25 28 31 34 37 40 43 46 49 52 55 58 61
Age (days after birth)
WT (n = 16)
SXR (n = 7)
VPSXR (n = 9)

FIG. 11

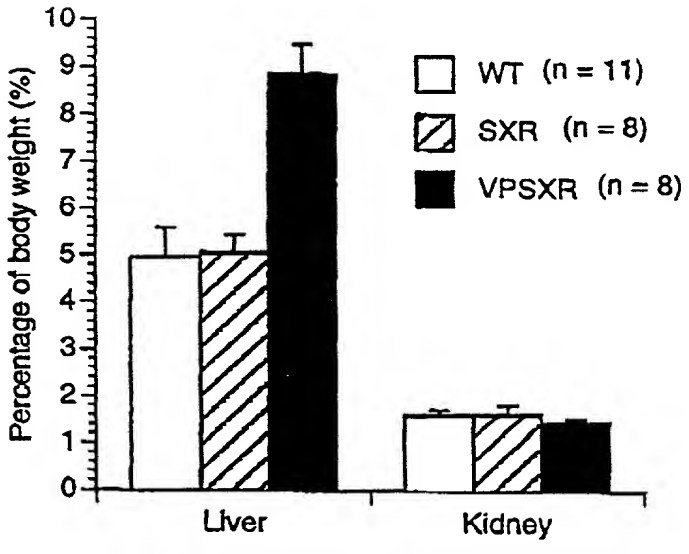
Percentage of body weight (%)
10
9
8
7
6
5
4
3
2
1
0
Liver
Kidney
WT (n = 11)
SXR (n = 8)
VPSXR (n = 8)

FIG. 12